

Appl. No.: 09/870,414

Amdt. dated 05/02/2005

Reply to Office action of November 30, 2004

Amendments to the Claims:

1. (Previously Presented) A method of treating an ulcer, comprising administering a therapeutic amount of a hydrogel matrix in liquid form to the ulcer, the matrix composition comprising gelatin and a long chain carbohydrate.
2. (Original) The method of Claim 1, wherein the matrix comprises about 0.01 to about 40 mM gelatin.
3. (Original) The method of Claim 1, wherein the gelatin comprises denatured collagen.
4. (Original) The method of Claim 1, wherein the long chain carbohydrate comprises dextran.
5. (Original) The method of Claim 4, wherein the matrix comprises about 0.01 to about 10 mM dextran.
6. (Original) The method of Claim 1, wherein the long chain carbohydrate has a molecular weight of about 20,000 to about 1,000,000 Daltons.
7. (Original) The method of Claim 1, wherein the matrix further comprises an effective amount of polar amino acids selected from the group consisting of arginine, lysine, histidine, glutamic acid, and aspartic acid.
8. (Original) The method of Claim 7, wherein the effective amount of polar amino acids comprises about 3 to about 150 mM of polar amino acids.
9. (Original) The method of Claim 7, wherein the effective amount of polar amino acids comprises about 10 to about 65 mM of polar amino acids.

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10. (Original) The method of Claim 7, wherein the polar amino acids are selected from the group consisting of arginine, glutamic acid, lysine and mixtures thereof.
11. (Original) The method according to claim 10, wherein the matrix comprises:
about 2 to about 60 mM of L-glutamic acid;
about 0.5 to about 30 mM of L-lysine; and
about 1 to about 40 mM of arginine.
12. (Original) The method of Claim 11, wherein the matrix comprises:
about 5 to about 40 mM of L-glutamic acid;
about 1 to about 15 mM of L-lysine; and
about 1 to about 30 mM of arginine.
13. (Original) The method according to claim 10, wherein the effective amount of polar amino acids comprises about 2 to about 60 mM of L-glutamic acid.
14. (Original) The method according to claim 10, wherein the effective amount of polar amino acids comprises about 1 to about 40 mM of arginine.
15. (Original) The method of Claim 10, wherein the effective amount of polar amino acids comprises about 0.5 to about 30 mM of L-lysine.
16. (Original) The method of Claim 1, wherein the matrix further comprises at least one nitric oxide inhibitor.
17. (Original) The method of Claim 16, wherein the nitric oxide inhibitor is selected from the group consisting of L-cysteine, L-arginine analogues, cystine, heparin, and mixtures thereof.

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18. (Original) The method of Claim 16, wherein the nitric oxide inhibitor is present in an amount of about 5 to about 1000 μM .

19. (Original) The method of Claim 16, wherein the nitric oxide inhibitor is present in an amount of about 20 to about 200 μM .

20. (Original) The method of Claim 1, wherein the matrix further comprises about 5 to about 500 μM of L-cysteine.

21. (Original) The method of Claim 20, wherein the matrix comprises about 15 to about 25 μM of L-cysteine.

22. (Original) The method of Claim 1, wherein the matrix further comprises about 5 to about 500 μM of an L-arginine analogue.

23. (Original) The method of Claim 22, wherein the L-arginine analogue comprises aminoguanidine.

24. (Original) The method of Claim 22, wherein the matrix comprises about 15 to about 25 μM of an L-arginine analogue.

25. (Original) The method of Claim 1, wherein the matrix further comprises a superoxide inhibitor.

26. (Original) The method of Claim 25, wherein the superoxide inhibitor comprises EDTA or a salt thereof.

27. (Original) The method of Claim 25, wherein the superoxide inhibitor is present in an amount of about 1 to about 8 mM.

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28. (Original) The method of claim 1, wherein the gelatin comprises denatured collagen and the long chain carbohydrate comprises dextran.

29. (Original) The method of Claim 1, wherein said administering step comprises injecting the matrix into one or more locations selected from the group consisting of locations within the ulcer, locations around the periphery of the ulcer, locations underneath the ulcer and combinations thereof.

30. (Original) The method of Claim 1, wherein the therapeutic amount comprises about 1.0 to about 60 ml.

31. (Original) The method of Claim 1, wherein the ulcer is a diabetic foot ulcer.

32. (Previously presented) A method of treating an ulcer, comprising administering a therapeutic amount of a hydrogel matrix to the ulcer, the matrix composition comprising denatured collagen, dextran, and an effective amount of polar amino acids selected from the group consisting of arginine, lysine, histidine, glutamic acid, aspartic acid, and mixtures thereof.

33. (Original) The method of Claim 32, wherein the effective amount of polar amino acids comprises about 3 to about 150 mM of polar amino acids.

34. (Original) The method of Claim 33, wherein the effective amount of polar amino acids comprises about 10 to about 65 mM of polar amino acids.

35. (Original) The method of Claim 32, wherein the polar amino acids are selected from the group consisting of arginine, glutamic acid, lysine and mixtures thereof.

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36. (Original) The method according to claim 35, wherein the matrix comprises:
about 2 to about 60 mM of L-glutamic acid;
about 0.5 to about 30 mM of L-lysine; and
about 1 to about 40 mM of arginine.

37. (Original) The method of Claim 32, wherein the matrix further comprises at least one nitric oxide inhibitor.

38. (Original) The method of Claim 37, wherein the nitric oxide inhibitor is selected from the group consisting of L-cysteine, L-arginine analogues, cystine, heparin, and mixtures thereof.

39. (Original) The method of Claim 37, wherein the nitric oxide inhibitor is present in an amount of about 5 to about 1000 μ M.

40. (Original) The method of Claim 37, wherein the nitric oxide inhibitor is present in an amount of about 20 to about 200 μ M.

41. (Original) The method of Claim 32, wherein the matrix further comprises about 5 to about 500 μ M of L-cysteine.

42. (Original) The method of Claim 32, wherein the matrix further comprises about 5 to about 500 μ M of an L-arginine analogue.

43. (Original) The method of Claim 32, wherein the matrix further comprises a superoxide inhibitor.

44. (Original) The method of Claim 43, wherein the superoxide inhibitor comprises BDTA or a salt thereof.

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45. (Original) The method of Claim 32, wherein said administering step comprises injecting the matrix into one or more locations selected from the group consisting of locations within the ulcer, locations around the periphery of the ulcer, locations underneath the ulcer and combinations thereof.

46. (Original) The method of Claim 32, wherein the ulcer is a diabetic foot ulcer.

47. (Original) The method of Claim 32, wherein said therapeutic amount comprises about 1.0 ml to about 60 ml.

48. (Previously presented) A method of treating an ulcer, comprising administering a therapeutic amount of a hydrogel matrix in liquid form to the ulcer, the matrix composition comprising denatured collagen, dextran, L-cysteine, and an effective amount of polar amino acids selected from the group consisting of arginine, lysine, histidine, glutamic acid, aspartic acid, and mixtures thereof.

49. (Original) The method of Claim 48, wherein said administering step comprises injecting the matrix into one or more locations selected from the group consisting of locations within the ulcer, locations around the periphery of the ulcer, locations underneath the ulcer and combinations thereof.

50. (Original) The method of Claim 48, wherein said therapeutic amount comprises about 1.0 mL to about 60 mL.

51. (Original) The method of Claim 48, wherein the ulcer is a diabetic foot ulcer.

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52. (Previously presented) A method of treating an ulcer, comprising administering a therapeutic amount of a hydrogel matrix in liquid form to the ulcer, the matrix composition comprising gelatin, a long chain carbohydrate having a molecular weight of about 20,000 to about 1,000,000 Daltons, and at least one polar amino acid, wherein said administering step comprises injecting the matrix into one or more locations selected from the group consisting of locations within the ulcer, locations around the periphery of the ulcer, locations underneath the ulcer, and combinations thereof.

53. (Previously presented) The method of Claim 52, wherein the ulcer is a foot ulcer resulting from diabetes-related vasculoneuropathy.

54. (New) The method of Claim 1, wherein said administering step comprises one or more injections of the matrix in the area of the dermal/subdermal tissue junction.

55. (New) The method of Claim 1, further comprising the step of debriding the ulcer prior to said administering step.